

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

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Claims 1-15 (Cancelled).

16. (Previously Presented) An isolated nucleic acid comprising the nucleotide sequence encoding the effector domain of the binding molecule as claimed in claim 32, wherein said nucleic acid is DNA.

17. (Previously Presented) An isolated nucleic acid comprising the nucleotide sequence encoding the binding molecule as claimed in claim 32, wherein said nucleic acid is DNA.

18. (Previously Presented) The nucleic acid as claimed in claim 16 which is a replicable vector.

19. (Previously Presented) The nucleic acid as claimed in claim 18 wherein the nucleotide sequence is operably linked to a promoter.

20. (Previously Presented) An isolated host cell comprising or transformed with the vector of claim 19.

21. (Currently Amended) A process for producing a binding molecule which is a recombinant polypeptide comprising:

(i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and

(ii) an effector domain having an amino acid sequence homologous to a constant domain of a human immunoglobulin heavy chain;

wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and the effector domain is capable of specifically binding Fc $\gamma$ RIIb and optionally FcRn,

and wherein the effector domain comprises a chimeric C<sub>H</sub>2 domain which is derived from two or more human immunoglobulin heavy chain C<sub>H</sub>2 domains, which human immunoglobulins are selected from IgG1, IgG2 and IgG4,

and wherein the effector domain has a reduced affinity for Fc $\gamma$ RI, Fc $\gamma$ RIIa and Fc $\gamma$ RIII and a reduced ability to mediate complement lysis by comparison with said

constant domain of a human immunoglobulin heavy chain;

the process comprising the steps of modifying a nucleotide sequence encoding a first human immunoglobulin heavy chain C<sub>H</sub>2 domain such that 2 or 3 amino acids in at least 1 region of the C<sub>H</sub>2 domain correspond to the amino acids from a second human immunoglobulin heavy chain C<sub>H</sub>2 domain,

wherein said modification introduces the following blocks of amino acids at the stated positions: 233P, 234V, 235A, 236G, 327G, 330S and 331S numbered with respect to the EU numbering system of Kabat

and wherein said chimeric C<sub>H</sub>2 domain is at least 98% identical to G1  $\Delta$ ac (SEQ ID NO:3) or G4  $\Delta$ c (SEQ ID NO:12) as shown in Figure 17

introducing into a host cell a vector comprising said modified nucleotide sequence, culturing said host cell under conditions such that said binding molecule is produced, and isolating said binding molecule from said cell culture.

22. (Cancelled).

23. (Previously Presented) A method of binding a target molecule, said method comprising contacting said target molecule with said binding molecule of claim 32 under conditions to allow binding.

24. (Previously Presented) The method of claim 23 wherein the effector domain specifically binds Fc $\gamma$ RIIb, which binding causes inhibition of one or more of B cell activation; mast cell degranulation; and phagocytosis.

25. (Previously Presented) The method of claim 23 to inhibit the binding of a second binding molecule to the target molecule.

26. (Previously Presented) The method of claim 25 wherein the second binding molecule is an antibody.

27. (Previously Presented) The method of claim 23 wherein the target molecule is selected from the group consisting of the RhD antigen of red blood cells; a human platelet antigen (HPA); a neutrophil antigen; a T-cell receptor; an integrin; a glomerular basement membrane (GBM) collagen type IV; a Der P1; VAP-1; laminin; lutheran; platelet glycoprotein VI; and platelet glycoprotein Ia/IIa.

28. (Previously Presented) The method of claim 23 wherein said target molecule is in a patient suffering from a disorder selected from the group consisting of:

- i) Graft-vs-host disease, host-vs-graft disease, organ transplant rejection, bone-marrow transplant rejection, autoimmune vasculitis, arthritis or asthma, wherein the target molecule is a T-cell receptor;
- ii) autoimmune haemolytic anaemia or autoimmune thrombocytopenia, wherein the target molecule is selected from the group consisting of red blood cell Rhesus antigens D,C,c,E and e, the Kell (K1) antigen and platelet glycoprotein GPIIb/IIIa and GPIb/IX/V;
- iii) foetal/neonatal alloimmune thrombocytopenia, wherein the target molecule is human platelet antigen (HPA)-1a or platelet glycoprotein IIIa;
- iv) dust mite allergy, wherein the target molecule is Der P1 protein of the house dust mite *Dermatophagoides pteronyssinus*;
- v) Crohn's, wherein the target molecule is VAP-1;
- vi) haemolytic disease of the newborn (HDN), wherein the target molecule is selected from the group consisting of red blood cell Rhesus antigens D,C,c,E and e, and the Kell (K1) antigen;

- vii) Goodpastures, wherein the target molecule is non-collagenous (NC1) domain of  $\alpha 3(\text{IV})$  collagen;
- viii) sickle cell anaemia, wherein the target molecule is selected from the group consisting of: thrombospondin, laminin and lutheran; and
- ix) coronary artery occlusion, wherein the target molecule is selected from the group consisting of integrin  $\alpha_2\beta_1$  (platelet glycoprotein Ia/IIa) and non-integrin platelet glycoprotein VI.

29. (Previously Presented) The method of claim 23 wherein the contacting step is a step of administering the binding molecule to a patient, or optionally to the mother of the patient where the patient is an unborn infant.

Claim 30 (Cancelled).

31. (Withdrawn) An oligonucleotide selected from:

MO22BACK: 5' TCT CCA ACA AAG GCC TCC CGT CCT CCA TCG AGA AAA 3' (SEQ ID NO:16)

MO22: 5' TTT TCT CGA TGG AGG ACG GGA GGC CTT TGT TGG AGA 3' (SEQ ID NO:17)

MO7BACK: 5' TCC TCA GCA CCT CCA GTC GCG GGG GGA CCG TCA GTC 3' (SEQ ID NO:18)

MO21: 5' GAC TGA CGG TCC CGC GAC TGG AGG TGC TGA GGA 3' (SEQ ID NO:19)

32. (Currently Amended) A binding molecule which is a recombinant polypeptide comprising:

(i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and

(ii) an effector domain having an amino acid sequence homologous to a constant domain of a human immunoglobulin heavy chain;

wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and the effector domain is capable of specifically binding Fc $\gamma$ RIIb and optionally FcRn,

and wherein the effector domain comprises a chimeric C<sub>H</sub>2 domain which is derived from two or more human immunoglobulin heavy chain C<sub>H</sub>2 domains, which human immunoglobulins are selected from IgG1, IgG2 and IgG4,

and wherein the effector domain has a reduced affinity for Fc $\gamma$ RI, Fc $\gamma$ RIIa and Fc $\gamma$ RIII and a reduced ability to mediate complement lysis by comparison with said constant domain of a human immunoglobulin heavy chain

and wherein the chimeric C<sub>H</sub>2 domain is a human immunoglobulin heavy chain C<sub>H</sub>2 domain which has the following blocks of amino acids at the stated positions: 233P, 234V, 235A, 236G, 327G, 330S and 331S numbered with respect to the EU numbering system of Kabat, and is at least 98% identical to G1  $\Delta$ c (SEQ ID NO:3) or G4  $\Delta$ c (SEQ ID NO:12) as shown in Figure 17.

33. (Previously Presented) The binding molecule as claimed in claim 32 wherein the chimeric C<sub>H</sub>2 domain consists of G1Δac (SEQ ID NO:3) or G4Δc (SEQ ID NO:12) as shown in Figure 17.

Claims 34-36 (Cancelled).

37. (Previously Presented) The binding molecule as claimed in claim 32 wherein the binding domain derives from a different source to the effector domain.

38. (Previously Previously) The binding molecule as claimed in claim 32 wherein the target molecule is selected from the group consisting of the RhD antigen of red blood cells; a human platelet antigen (HPA); a neutrophil antigen; a T-cell receptor; an integrin; a glomerular basement membrane (GBM) collagen type IV; a Der P1; VAP-1; laminin; lutheran; platelet glycoprotein VI; and platelet glycoprotein Ia/IIa.

39. (Previously Presented) The binding molecule as claimed in claim 38 wherein the binding domain is the binding site of an antibody selected from the group consisting of anti-CD52; anti-RhD; anti-HPA-1a; anti-VAP-1; murine anti-α3 (IV) NC1; anti-CD3; anti-Der p I; anti-laminin; and anti-lutheran.

40. (Previously Presented) A preparation comprising the binding molecule as claimed in claim 32 plus a pharmaceutically acceptable carrier.

41. (Currently Amended) A binding molecule which is a recombinant polypeptide comprising:

(i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and

(ii) an effector domain having an amino acid sequence homologous to a constant domain of a human immunoglobulin heavy chain;

wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and the effector domain is capable of specifically binding Fc $\gamma$ RIIb and optionally FcRn,

and wherein the effector domain comprises a chimeric C<sub>H</sub>2 domain which is derived from two or more human immunoglobulin heavy chain C<sub>H</sub>2 domains, which human immunoglobulins are selected from IgG1, IgG2 and IgG4,

and wherein the effector domain has a reduced affinity for Fc $\gamma$ RI, Fc $\gamma$ RIIa and Fc $\gamma$ RIII and a reduced ability to mediate complement lysis by comparison with said constant domain of a human immunoglobulin heavy chain

and wherein the chimeric C<sub>H</sub>2 domain is a human immunoglobulin heavy chain C<sub>H</sub>2 domain which has the following blocks of amino acids at the stated positions: 233P, 234V, 235A and no residue at 236, 327G, 330S and 331S, numbered with respect to the EU system of Kabat, and is at least 98% identical to G1  $\Delta$ ab (SEQ ID NO:1) or G2  $\Delta$ a (SEQ ID NO:2) as shown in Figure 17.

42. (Currently Amended) ~~The binding molecule as claimed in claim 41~~ A binding molecule which is a recombinant polypeptide comprising:



(i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and

(ii) an effector domain having an amino acid sequence homologous to a constant domain of a human immunoglobulin heavy chain;

wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and the effector domain is capable of specifically binding Fc $\gamma$ RIIb and optionally FcRn,

and wherein the effector domain comprises a chimeric C<sub>H</sub>2 domain which is derived from two or more human immunoglobulin heavy chain C<sub>H</sub>2 domains, which human immunoglobulins are selected from IgG1, IgG2 and IgG4,

and wherein the effector domain has a reduced affinity for Fc $\gamma$ RI, Fc $\gamma$ RIIa and Fc $\gamma$ RIII and a reduced ability to mediate complement lysis by comparison with said constant domain of a human immunoglobulin heavy chain

and wherein the chimeric C<sub>H</sub>2 domain is a human immunoglobulin heavy chain C<sub>H</sub>2 domain which has the following blocks of amino acids at the stated positions: 233P, 234V, 235A and no residue at 236, 327G, 330S and 331S, numbered with respect to the EU system of Kabat, and is at least 98% identical to G1  $\Delta$ ab (SEQ ID NO:1) or G2  $\Delta$ a (SEQ ID NO:2) as shown in Figure 17,

wherein the chimeric C<sub>H</sub>2 domain consists of G1 $\Delta$ ab (SEQ ID NO:1) or G2 $\Delta$ a (SEQ ID NO:2) as shown in Figure 17.

Claims 43-45 (Cancelled).

46. (Previously Presented) The binding molecule as claimed in claim 41 wherein the binding domain derives from a different source to the effector domain.

47. (Previously Presented) The binding molecule as claimed in claim 41 wherein the target molecule is selected from the group consisting of the RhD antigen of red blood cells; a human platelet antigen (HPA); a neutrophil antigen; a T-cell receptor; an integrin; a glomerular basement membrane (GBM) collagen type IV; a Der P1; VAP-1; laminin; lutheran; platelet glycoprotein VI; and platelet glycoprotein Ia/IIa.

48. (Previously Presented) The binding molecule as claimed in claim 47 wherein the binding domain is the binding site of an antibody selected from the group consisting of anti-CD52; anti-RhD; anti-HPA-1a; anti-VAP-1; murine anti- $\alpha$ 3 (IV) NC1; anti-CD3; anti-Der p I; anti-laminin; and anti-lutheran.

49. (Previously Presented) A preparation comprising the binding molecule as claimed in claim 41 plus a pharmaceutically acceptable carrier.

50. (Previously Presented) An isolated nucleic acid comprising the nucleotide sequence encoding the effector domain of the binding molecule as claimed in claim 41, wherein said nucleic acid is DNA.

51. (Previously Presented) An isolated nucleic acid comprising the nucleotide sequence encoding the binding molecule as claimed in claim 41, wherein said nucleic acid is DNA.

52. (Previously Presented) The nucleic acid as claimed in claim 50 which is a replicable vector.

53. (Previously Presented) The nucleic acid as claimed in claim 52 wherein the nucleotide sequence is operably linked to a promoter.

54. (Previously Presented) An isolated host cell comprising or transformed with the vector of claim 53.

55. (Currently Amended) A process for producing a binding molecule which is a recombinant polypeptide comprising:

(i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and

(ii) an effector domain having an amino acid sequence homologous to a constant domain of a human immunoglobulin heavy chain;

wherein the binding molecule is capable of binding the target molecule without triggering significant complement dependent lysis, or cell mediated destruction of the target, and the effector domain is capable of specifically binding Fc $\gamma$ RIIb and optionally FcRn,

and wherein the effector domain comprises a chimeric C<sub>H</sub>2 domain which is derived from two or more human immunoglobulin heavy chain C<sub>H</sub>2 domains, which human immunoglobulins are selected from IgG1, IgG2 and IgG4,

and wherein the effector domain has a reduced affinity for FcγRI, FcγRIIa and FcγRIII and a reduced ability to mediate complement lysis by comparison with said constant domain of a human immunoglobulin heavy chain;

the process comprising the steps of modifying a nucleotide sequence encoding a first human immunoglobulin heavy chain C<sub>H</sub>2 domain such that 2, 3 or 4 amino acids in at least 1 region of the C<sub>H</sub>2 domain correspond to the amino acids from a second human immunoglobulin heavy chain C<sub>H</sub>2 domain,

wherein said modification introduces the following blocks of amino acids at the stated positions: 233P, 234V, 235A and no residue at 236 and 327G, 330S and 331S numbered with respect to the EU numbering system of Kabat

and wherein said chimeric C<sub>H</sub>2 domain is at least 98% identical to G1  $\Delta$ ab (SEQ ID NO:1) or G2  $\Delta$ a (SEQ ID NO:2) as shown in Figure 17

introducing into a host cell a vector comprising said modified nucleotide sequence,  
culturing said host cell under conditions such that said binding molecule is produced, and  
isolating said binding molecule from said cell culture.

56. (Previously Presented) The process as claimed in claim 55 wherein 2 amino acids in 1 region of the C<sub>H</sub>2 domain are modified to the corresponding amino acids from the second human immunoglobulin heavy chain C<sub>H</sub>2 domain.

57. (Previously Presented) A method of binding the target molecule, said method comprising contacting said target molecule with said binding molecule of claim 41 under conditions to allow binding.

58. (Previously Presented) The method of claim 57 wherein the effector domain specifically binds FcγRIIb, which binding causes inhibition of one or more of B cell activation; mast cell degranulation; and phagocytosis.

59. (Previously Presented) The method of claim 57 to inhibit the binding of a second binding molecule to the target molecule.

60. (Previously Presented) The method of claim 59 wherein the second binding molecule is an antibody.

61. (Previously Presented) The method of claim 57 wherein the target molecule is selected from the group consisting of the RhD antigen of red blood cells; an HPA alloantigen of platelets; a neutrophil antigen; a T-cell receptor; integrin; GBM collagen; Der P1; HPA-1a; VAP-1; laminin; lutheran; platelet glycoprotein VI; and platelet glycoprotein Ia/IIa.

62. (Previously Presented) The method of claim 57 wherein said target molecule is in a patient suffering from a disorder selected from the group consisting of:

- i) Graft-vs-host disease, host-vs-graft disease, organ transplant rejection, bone-marrow transplant rejection, autoimmune vasculitis, arthritis or asthma, wherein the target molecule is a T-cell receptor;
- ii) autoimmune haemolytic anaemia or autoimmune thrombocytopenia, wherein the target molecule is selected from the group consisting of red blood cell Rhesus antigens D,C,c,E and e, the Kell (K1) antigen and platelet glycoprotein GPIIb/IIIa and GPIb/IX/V;
- iii) foetal/neonatal alloimmune thrombocytopenia, wherein the target molecule is human platelet antigen (HPA)-1a or platelet glycoprotein IIIa;
- iv) dust mite allergy, wherein the target molecule is Der P1 protein of the house dust mite *Dermatophagoides pteronyssinus*;
- v) Crohn's, wherein the target molecule is VAP-1;
- vi) haemolytic disease of the newborn (HDN), wherein the target molecule is selected from the group consisting of red blood cell Rhesus antigens D,C,c,E and e, and the Kell (K1) antigen;
- vii) Goodpastures, wherein the target molecule is non-collagenous (NC1) domain of  $\alpha 3(\text{IV})$  collagen;
- viii) sickle cell anaemia, wherein the target molecule is selected from the group consisting of: thrombospondin, laminin and lutheran; and
- ix) coronary artery occlusion, wherein the target molecule is selected from the group consisting of integrin  $\alpha_2\beta_1$  (platelet glycoprotein Ia/IIa) and non-integrin platelet glycoprotein VI.

63. (Previously Presented) The method of claim 57 wherein the contacting step is a step of administering the binding molecule to a patient, or optionally to the mother of the patient where the patient is an unborn infant.

64. (Previously Presented) The binding molecule as claimed in claim 39 wherein the anti-CD52 binding domain is CAMPATH-1; the anti-RhD is FOG1; the anti-Der p I is 2C7; the anti-CD3 is YTH12.5.

65. (Previously Presented) The binding molecule as claimed in claim 48 wherein the anti-CD52 binding domain is CAMPATH-1; the anti-RhD is FOG1; the anti-Der p I is 2C7; the anti-CD3 is YTH12.5.

66.-67. (Cancelled).

68. (Previously Presented) The method as claimed in claim 27 wherein the HPA is HPA-1a.

69. (Previously Presented) The binding molecule as claimed in claim 38 wherein the HPA is HPA-1a.

70. (Previously Presented) The binding molecule as claimed in claim 47 wherein the HPA is HPA-1a.

71. (Previously Presented) A binding molecule which is a recombinant polypeptide comprising:

(i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and

(ii) an effector domain comprising chimeric C<sub>H</sub>2 domain which consists of G1Δac (SEQ ID NO:3) as shown in Figure 17.

72. (Previously Presented) A binding molecule which is a recombinant polypeptide comprising:

(i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and

(ii) an effector domain comprising chimeric C<sub>H</sub>2 domain which consists of G4Δc (SEQ ID NO:12) as shown in Figure 17.

73. (Previously Presented) A binding molecule which is a recombinant polypeptide comprising:

(i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and

(ii) an effector domain comprising chimeric C<sub>H</sub>2 domain which consists of G1Δab (SEQ ID NO:1) as shown in Figure 17.

74. (Previously Presented) A binding molecule which is a recombinant polypeptide comprising:



(i) a binding domain capable of binding a target molecule, which binding domain is the binding site of an antibody, and

(ii) an effector domain comprising chimeric C<sub>H</sub>2 domain which consists of G2Δa (SEQ ID NO:2) as shown in Figure 17.

75. (Previously Presented) An isolated nucleic acid comprising the nucleotide sequence encoding the effector domain of the binding molecule as claimed in claim 71, wherein said nucleic acid is DNA.

76. (Previously Presented) An isolated nucleic acid comprising the nucleotide sequence encoding the effector domain of the binding molecule as claimed in claim 72, wherein said nucleic acid is DNA.

77. (Previously Presented) An isolated nucleic acid comprising the nucleotide sequence encoding the effector domain of the binding molecule as claimed in claim 73, wherein said nucleic acid is DNA.

78. (Previously Presented) An isolated nucleic acid comprising the nucleotide sequence encoding the effector domain of the binding molecule as claimed in claim 74, wherein said nucleic acid is DNA.